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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/657,199	09/09/2003	Chin-Chu Chen	MR2723-307	9131

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EXAMINER	
HANLEY, SUSAN MARIE	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/657,199	CHEN ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 September 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-4, in the reply filed on 4/7/06 is acknowledged. Claims 5-7 have been cancelled.

Claims 1-4 are presented for examination.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
The name and signature for Inventor Ying-Shih Feng do not match. The signature for Inventor Feng is "Paul Feng". The signature does not match the official name.

Drawings

The drawings are objected to under 37 CFR 1.83(a). Fig. 12 depicts a beta-lactam structure that is missing a bond between the ring and the methoxy group. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the

brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing the beta-lactam antibiotics, M-4, A-3-2 and 3-3-A-2, from a protoplast fusion strain CCRC 930060 which is obtained by fusing the protoplasts of *Penicillium chrysogeum* (ATCC 48271) and *Cephalosporium acremonium* (CCRC 31697), does not reasonably provide enablement for a method of producing any possible beta-lactam antibiotic from a protoplast fusion strain which is obtained by fusing the protoplasts of any strain of *Penicillium chrysogeum* with any strain of *Cephalosporium acremonium*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are drawn to a method for producing any possible beta-lactam antibiotic from a protoplast fusion strain which is obtained by fusing the protoplasts of any strain of *Penicillium chrysogeum* with any strain of *Cephalosporium acremonium*. The specification shows that microorganisms belonging to the strains *Penicillium chrysogeum* (ATCC 48271) and *Cephalosporium acremonium* (CCRC 31697) are capable of undergoing protoplast fusion to make the strain CCRC 930060 which synthesizes the beta-

lactam antibiotics M-4, A-3-2 and 3-3-A-2. The limited showing of two bacterial strains that can produce a fusion protoplast with a particular activity is not sufficient to enable a claim drawn to a method for producing any possible beta-lactam antibiotic from a protoplast fusion strain obtained from the combination of any strain of all *Penicillium chrysogeum* and *Cephalosporium acremonium*..

The specification does not disclose if one skilled in the art can utilize any strain of *Penicillium chrysogeum* and *Cephalosporium acremonium* microorganism to make any possible fusion protoplast to synthesize any beta-lactam antibiotic with a reasonable expectation of results. Applicants point out that Dr. Elander was unable to achieve fusion strains from the combination of several strains of *Cephalosporium acremonium* and *Penicillium chrysogeum* that synthesized the desired antibiotics. In fact, Dr. Elander (Chang et al. (1982)) report that they tested a number of each of the *Cephalosporium acremonium* and *Penicillium chrysogeum* strains to make the protoplast fusion product (p. 22, Table 1). They obtained few stable hybrid isolates, none of which produced the desired antibiotics (p. 28, lst paragraph). The specification states, "However, through profound studies for many years, the present inventors obtain the fusion strain *of Penicillium chrysogeum* and *Cephalosporium acremonium*, and isolate the novel beta-lactam antibiotic" (p. 2). Hence, it is highly desirable obtain a fusion protoplast strain to synthesize antibiotics. However, the specification and the prior art disclose that the method of obtaining a fusion protoplast from the combination of *Penicillium chrysogeum* and *Cephalosporium acremonium* to produce beta-lactam antibiotics is rare and an individual characteristic of said strains. Furthermore, a search of the Registry database showed that compounds 3-3-A-2 and M-4 are novel compounds while A-3-2 has only been reported nine times in the literature. Neither *Penicillium chrysogeum* (ATCC 48271) nor *Cephalosporium acremonium* (CCRC 31697) have been reported to make any other claimed compounds individually. Hence, one skilled in the art would be unable to pick a strain from *Penicillium chrysogeum* and *Cephalosporium acremonium* and expect it to produce any particular antibiotic, much less novel compounds 3-3-A-2 and M-4 or little-reported A-3-2. If the method of claim 1 is not generally applicable to any species of *Penicillium chrysogeum* and *Cephalosporium Acremonium*, or a fusion protoplast thereof, or

any possible beta-lactam, then the desired synthetic activity all possible species of *Penicillium chrysogeum* and *Cephalosporium acremonium* and all possible known and unknown beta-lactams would be considered individually. This would be considered undue experimentation.

There is no reliable method that predicts which strains of *Penicillium chrysogeum* and *Cephalosporium acremonium* or fusion protoplast thereof have the desired activity described in the specification. Applicants acknowledge the difficulty in fusing *Penicillium chrysogeum* and *Cephalosporium acremonium* to make a viable protoplast that makes certain beta-lactam antibiotics. The specification does not teach how one of ordinary skill in the art could decide *a priori* which sources will provide *Penicillium chrysogeum* and *Cephalosporium acremonium* microorganisms or a fusion protoplast thereof with the desired characteristics. The limited disclosure cannot be extrapolated by the skilled artisan to predict which strains from *Penicillium chrysogeum* and *Cephalosporium Acremonium* or fusion protoplast thereof are capable of producing the compounds 3-3-A-2 and M-4 or little-reported A-3-2. It would require one of ordinary skill in the art undue experimentation to determine what species or strains of *Penicillium chrysogeum* and *Cephalosporium acremonium* or fusion protoplast thereof are capable of producing the compounds 3-3-A-2 and M-4 or little-reported A-3-2 according to the directions of the instant disclosure. Thus, claims 1-4 are not commensurate in scope with the enabling disclosure.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1-4 are drawn to a method for preparing penicillin/cephalosporin derivatives as described in claim 1 with a protoplast fusion strain obtained by culturing *Penicillium chrysogeum* (ATCC 48271) and *Cephalosporium acremonium* (CCRC 31697).

The disclosed microorganisms are essential to the claimed invention because it appears that only the fusion product of these particular strains can produce the desired antibiotics. According to the

specification, previous attempts by Dr. Elander to achieve strains by fusing the protoplasts of *Cephalosporium acremonium* and *Penicillium chrysogeum* did not results in fused protoplast that synthesized the desired antibiotics. In fact, Dr. Elander (Chang et al. (1982)) report that they tested a number of each of the *Cephalosporium acremonium* and *Penicillium chrysogeum* strains to make the protoplast fusion product (p. 22, Table 1). They obtained few stable hybrid isolates, none of which produced the desired antibiotics (p. 28, lst paragraph). Therefore, the disclosed strains of the microorganisms are needed to make the desired protoplast fusion product and they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public.

A search of the prior art and the ATCC catalog revealed that the *Penicillium* strain is commercially available from ATCC. Thus, it is enabled. However, neither the specification nor the prior art disclose if the *C. acremonium* strain was deposited by Applicant or if it is commercially available. In fact, a Web search for the microorganism revealed that CCRC is an old acronym for the depository of the Food Industry Research Institute. The new acronym for their depository is "BCRC". A search of the BCRC website did not reveal the *Cephalosporium acremonium* (CCRC 31697) strain. Thus, neither the specification nor the prior art describe how to obtain this strain which is necessary to prepare the protoplast fusion strain. As stated *supra*, the *Penicillium* strain is available to the public. However, the instant invention is not enabled because the specification does not teach the skilled artisan would obtain the *Cephalosporium acremonium* (CCRC 31697) strain which is necessary to obtain the specific protoplast fusion product disclosed by the specification.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1-4 are drawn to a method for preparing penicillin/cephalosporin derivatives as described in claim 1 with a protoplast fusion strain, CCRC

930060, obtained by culturing *Penicillium chrysogeum* (ATCC 48271) and *Cephalosporium acremonium* (CCRC 31697).

If Applicant has deposited the *Cephalosporium acremonium* (CCRC 31697) strain, the specification does not disclose a repeatable process to obtain the microorganisms and it is not apparent if the microorganisms are readily available to the public. Likewise, it appears that the protoplast fusion strain, CCRC 930060, is unique in its ability to produce the desired antibiotics and is not obtainable by a repeatable process. As discussed *supra*, Dr. Elander was unable to achieve fusion strains from the combination of several strains of *Cephalosporium acremonium* and *Penicillium chrysogeum* that synthesized the desired antibiotics. In fact, Dr. Elander (Chang et al. (1982)) report that they tested a number of each of the *Cephalosporium acremonium* and *Penicillium chrysogeum* strains to make the protoplast fusion product (p. 22, Table 1). They obtained few stable hybrid isolates, none of which produced the desired antibiotics (p. 28, lst paragraph). The instant specification does not teach the ordinary artisan how to select hyphas that will reliably produce the desired antibiotics. Thus, the specification does not disclose a repeatable process to obtain the protoplast fusion strain, CCRC 930060, and it is not apparent if the said strain is readily available to the public.

For the CCRC 31697 microorganism and the protoplast fusion strain, CCRC 930060, the specification must contain the date that the microorganism was deposited, the accession number for the microorganism, the name of the microorganism and the address of where the microorganism was deposited. *If the deposit is made under the terms of the Budapest Treaty*, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or hers signature and registration number, **stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent**, would satisfy the deposit requirement made herein.

*If the deposit has **not** been made under the Budapest Treaty*, then in order to certify that the deposit meets the criteria set forth in CFR 1.801-809, applicants may provide assurance of compliance by an

affidavit or declaration, or by a statement by an attorney of record over his or hers signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) a restriction upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and,

(d) the deposit will be replaced if it should ever become inviable.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected because the phrase "the residues are repeatedly treated with the above steps for two times" is vague and indefinite. It is unclear which two steps are to be repeated because there are more than two steps that are "above".

Claims 2-4 are rejected because the use of the designations 3-3-A-2 and M-4 or little-reported A-3-2 to describe specific compounds is vague and indefinite. The indicated designations are not art-recognized terms. Neither do they provide any structural information that distinguishes the compounds from each other or the prior art. It is suggested that the claims include the structures of the compounds or that the claims refers to the compound of Fig. 8, 12 or 14 in order to specifically define what structure is being claimed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Susan Hanley
Patent Examiner
1651